Answer 1:

Bibliographic Information

Human osteosarcoma xenografts and their sensitivity to chemotherapy. Bruheim, Skjalg; Bruland, Oyvind S.; Breistol, Knut; Maelandsmo, Gunhild M.; Fodstad, Oystein. Department of Tumor Biology, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo, Norway. Pathology Oncology Research (2004), 10(3), 133-141. Publisher: Aranyi Lajos Foundation, CODEN: POREFR ISSN: 1219-4956. Journal written in English. CAN 142:253924 AN 2004:1018322 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Despite the increased survival rates of osteosarcoma patients attributed to adjuvant chemotherapy, at least one third of the patients still die due to their disease. Further improvements in the management of osteosarcoma may rely on a more individualized treatment strategy, as well as on the introduction of new drugs. To aid in the preclin. evaluation of new candidate substances against osteosarcoma, we have established 11 human osteosarcoma xenograft lines and characterized them with regard to response to five different ref. drugs. Doxorubicin, cisplatin methotrexate, ifosfamide and lomustine were effective in 3/11, 3/11,1/10, 5/11 and 4/11 of the xenografts, resp. Five xenografts were resistant to all compds. tested. We also assessed the mRNA expression levels of the xenografts for the O6-Methylguanine DNA Methyltransferase (MGMT), DNA topoisomerase II- (Topo II)-α, Gluthathione-S-transferase (GST)-π, Multidrug-resistance related protein (MRP) 1 and Multidrug-resistance (MDR) 1 genes. There was an inverse correlation between the transcript levels of GST-π and doxorubicin growth inhibition ($r = -0.66$; $p<0.05$), and between the transcript levels of MGMT and the effect of lomustine ($r = -0.72$; $p<0.01$), whereas the expression of MRP1 and cisplatin growth inhibition was pos. correlated ($r=0.82$; $p<0.005$). This panel of xenografts should constitute a good tool for pharmacol. and mol. studies in osteosarcoma.

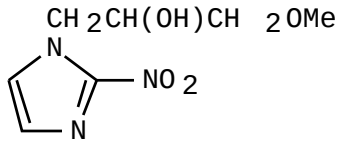
Answer 2:

Bibliographic Information

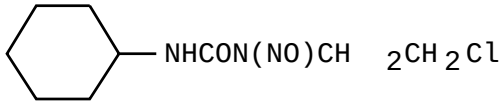
Modification of CCNU pharmacokinetics by misonidazole - a major mechanism of chemosensitization in mice. Lee, F. Y. F.; Workman, P. MRC Clin. Oncol. Radiother. Unit, MRC Cent., Cambridge, UK. British Journal of Cancer (1983), 47(5), 659-69. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 99:63957 AN 1983:463957 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effect of misonidazole (MISO)(I) [13551-87-6] on the pharmacokinetics of 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU)(II) [13010-47-4] was studied in mice. CCNU and its monohydroxylated metabolites were measured using a high performance liq. chromatog. method. In the absence of MISO the plasma disappearance of CCNU was biphasic with a $t1/2\alpha$ of 2.3 min and a $t1/2\beta$ of 53 min. The monohydroxylated metabolites of CCNU also followed biphasic clearance kinetics. A large single dose of MISO (0.5 mg/kg), given i.p. 30 min prior to CCNU, prolonged the $t1/2\alpha$ by a factor of 2.6 but had no effect on $t1/2\beta$. In addn., the apparent vol. of distribution was decreased by a factor of 1.6. Consequently, the plasma area under the curve ($AUC0-\infty$) was increased by a factor of 1.7 for CCNU and by a factor of 2.0 for total nitrosourea (CCNU + monohydroxylated metabolites). The effects of MISO on CCNU kinetics were dependent on MISO dose and plasma concn. and on the interval between MISO and CCNU administration. The concn. of CCNU was measured in 4 tumors: the KHT, RIF-1 and EMT6 mouse tumors, and the HT29 xenograft. For all 4 tumors, 0.5 mg/g MISO raised the tumor concns. of CCNU and total nitrosourea by a considerable amt. (2-2.5 times). More detailed studies in the KHT tumor demonstrated that there was a significant lag period before peak tumor CCNU concns. were reached, and that MISO increased the peak concns. by a factor of about 2.4. In contrast, there was no such lag period for the plasma, and MISO did not increase the plasma peak CCNU concns. Modification of the pharmacokinetics may be a major contributory factor in the enhancement of CCNU cytotoxicity by large single doses of MISO in vivo.



I



II

Answer 3:

Bibliographic Information

In vitro sensitivity of human melanoma xenografts to cytotoxic drugs. Correlation with in vivo chemosensitivity. Tveit, Kjell Magne; Fodstad, Oeystein; Olsnes, Sjur; Pihl, Alexander. Norwegian Cancer Society, Norsk Hydro's Inst. Cancer Res., Oslo, Norway. International Journal of Cancer (1980), 26(6), 717-22. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 94:76807 AN 1981:76807 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Single-cell suspensions prepd. from 5 human melanomas, grown serially as xenografts in athymic nude mice, were exposed in vitro to increasing concns. of dacarbazine [4342-03-4], CCNU [13010-47-4], procarbazine [671-16-9], vinblastine [865-21-4], and the cancerostatic lectins abrin and ricin. The in vitro chemosensitivity of the cells, as measured by the drug concns. required to inhibit colony formation in soft agar by 50%, was correlated with the growth delay of the xenografts in vivo, previously obsd. after treatment of the animals with maximal tolerable doses of the same drugs. For each drug, the in vitro sensitivity of the different xenografts was strongly correlated with their response in vivo. Apparently, the soft agar test, as carried out here, adequately reflects the relative sensitivity of the xenografts in vivo. The data indicate that human xenografts may be used to develop quant. in vitro chemosensitivity tests.

Answer 4:

Bibliographic Information

Comparison of antitumor activities of nitrosourea derivatives against mammary breast carcinoma (MX-1) in nude mice. Inoue, Katsuhiro; Fujimoto, Shuichi; Ogawa, Makoto. Div. Clin. Chemother., Cancer Chemother. Cent., Tokyo, Japan. Gann (1980), 71(5), 686-91. CODEN: GANNA2 ISSN: 0016-450X. Journal written in English. CAN 94:273 AN 1981:273 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activities of 6 nitrosourea derivs. against the xenograft of mammary breast carcinoma transplanted in nude mice (MX-1) were evaluated. A single treatment with ACNU [55661-38-6] (40 mg/kg, i.v.) induced 92% tumor regression, compared to 73% and 69% tumor regression induced by MCNU [58994-96-0] (15 mg/kg, i.v.) and CCNU [13010-47-4] (50 mg/kg, i.v.), resp. GANU [58484-07-4], 2-[3-2-chloroethyl)-3-nitrosoureido]-2-deoxyl-D-glucopyranose (DCNU) [54749-90-5], and 1-(2-chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea (MeCCNU) [13909-09-6] were less effective. To evaluate the antitumor activity of the drugs, the predetd. dose lethal to 0.10 of the BDF1 mice (LD10) was employed for each drug as a std. therapeutic dose to nude mice; doses higher than LD10 and 0.25 or 0.50 of the LD10 were also give. Apparently, the LD10 in BDF1 mice could be employed as a std. therapeutic dose in the chemotherapy of nude mice.

Answer 5:

Bibliographic Information

The combination of methyl-CCNU and irradiation: cell survival studies on a human tumor xenograft. Bateman, Angela E.; Fu, Karen K.; Towse, G. D. W. Radiother. Res. Dep., Inst. Cancer Res., Sutton/Surrey, UK. International Journal of Radiation Oncology, Biology, Physics (1979), 5(9), 1545-8. CODEN: IOBPD3 ISSN: 0360-3016. Journal written in English. CAN 92:69674 AN 1980:69674 CAPLUS

Abstract

Methyl-CCNU [13909-09-6] 3 h before γ-irradn. was the most effective time schedule of those tested on a human tumor xenograft in mice. This pretreatment decreased the D0 of the radiation survival curve from 231 to 135 rad without any effect on the shoulder of the curve.